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EXAMINER	
BAUSCH, SARAE L	
ART UNIT	**PAPER NUMBER**
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/055,728	VAN DER KUYL ET AL.	
	Examiner	Art Unit	
	Sarae Bausch	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *7,13,25-28,35-37 and 39-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-12,14-24,29-34 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group I, claims 1-24, 29-34, and 38, in the reply filed on 8/19/2004 is acknowledged. The election of one sequence is traversed by the Applicant's because "the Commissioner has decided *sua sponte* to partially waive the requirements of 37 CFR 1.141 *et seq.* and permit a reasonable number of such nucleotide sequences to be claimed in a single application" and MPEP 2434 allowing "in most cases, up to 10 independent and distinct nucleotide sequences" can be examined in a single application. This traversal has been thoroughly reviewed but not found persuasive because "up to 10" sequences does not require that 10 sequences be search. In this instance, searching more than 1 of 82 patentably distinct nucleic acids present a serious search burden for the office. Furthermore, searching the six sequences requested by the applicant creates a search burden for the office as each sequence represents patentable distinct nucleic acids that encode for different proteins even if they are related by being involved in angiogenesis, furthermore angiogenesis is a complex process that involves many steps and each sequence presented could be involved in different steps within the process. The requirement is still deemed proper and is therefore made FINAL.

2. Applicant's election without traverse of group I, claims 1-12, 14-24, 29-34, and 38 in a second restriction requirement filed on 11/22/2004 is acknowledged.

3. Claims 7, 13, 25-28, 35-37, and 39-41 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 12, 19, 33, and 38 are vague and indefinite.

(a). Claim 1 is drawn to a method for determining whether a treatment is effective in changing a status of a certain set of target cells in an individual. However, the final process step is determining whether the sample comprises an expression product of at least one marker gene. Accordingly, it is unclear as to whether the claim is intended to be limited to determining whether a sample comprises an expression product of one marker gene or for determining whether a treatment is effective in changing a status of certain set of target cells in an individual as referred to in the preamble. Applicants should amend the claim to indicate how the step of a determining whether a sample comprises an expression product of at least one marker gene results in determining the efficacy of treatment in changing a status of a certain set of target cells.

(b). Claim 12 is drawn to method of detecting an expression product of a marker gene, however the final process step is determining whether said nucleic acid hybridizes in said sample. Accordingly, it is unclear as to whether the claim is intended to be limited to determining whether a nucleic acid hybridizes in a sample or for detecting an expression product of a marker gene, as referred to in the preamble. Applicants should amend the claim to indicate how the step of determining whether a nucleic acid hybridizes in a sample results in detecting an expression product of a marker gene.

(c). Claim 19 is drawn to a method of determining whether an individual possesses a tumor cell and/or site of angiogenesis, however the final process step is determining whether a

sample comprises an expression product of at least one marker gene. Accordingly, it is unclear as to whether the claim is intended to be limited to determining whether a sample comprise an expression product of at least one marker gene or for determining whether an individual possesses a tumor cell and/or site of angiogenesis, as referred to in the preamble. Applicants should amend the claim to indicate how the step of determining whether a sample comprises an expression product of at least one marker gene results in a determining whether an individual possesses a tumor cell and/or site of angiogenesis.

(d). Claim 33 is drawn to a method of determining the presence of a tumor cell in an individual, however the final process step is detecting the level of peripheral blood mononuclear cell expression of at least one of SEQ ID Nos. Accordingly, it is unclear as to whether the claim is intended to be limited to detecting the level of peripheral blood mononuclear cell expression of at least one of SEQ ID Nos or for determining the presence of a tumor cell in an individual, as referred to in the preamble. Applicants should amend the claim to indicate how the step of detecting the level of peripheral blood mononuclear cell expression of at least one of SEQ ID Nos results in determining the presence of a tumor cell in an individual.

(e). Claim 38 is drawn to a method of determining whether an individual possesses a tumor cell and/or site of angiogenesis, however the final process step is quantifying an expression product of at least one marker gene in a sample. Accordingly, it is unclear as to whether the claim is intended to be limited to quantifying an expression product of at least one marker gene in a sample or for determining whether an individual possesses a tumor cell and/or site of angiogenesis, as referred to in the preamble. Applicants should amend the claim to indicate how the step of quantifying an expression product of at least one marker gene in a

sample results in determining whether an individual possesses a tumor cell and/or site of angiogenesis.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-6, 8-12, 14-24, 29-34, and 38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and the breadth of the claims

The claims are broadly drawn to a method of determining efficacy of treatment by a change in the status of target cells by obtaining a sample after initiating treatment and determining whether sample comprises expression product of at least one marker gene. The methods are further drawn to target cells comprising tumor cells and tumor cells that comprise

Kaposi's Sarcoma, samples comprising blood samples and peripheral blood mononuclear cells obtained within one week and two days of initiating treatment, and a marker gene that is quantified and comprises genes involved in generation, maintenance, and/or breakdown of blood vessels. The claims are also drawn to a method of detecting an expression product of a marker gene comprising obtaining a sample, introducing a nucleic acid into the sample, and determining whether the nucleic acid hybridizes to the sample and are further drawn to a tumor cell, comprising Kaposi's Sarcoma, and a site of angiogenesis. Claims are also drawn to a method of determining whether an individual possesses a non-hemopoetic tumor cell and/or site of angiogenesis by determining whether a hemopoetic cell from individual comprise an altered amount of expression product of a marker gene as compared to a reference value, and further drawn to a marker gene involved in angiogenesis and a hemopoietic cell comprising a peripheral blood mononuclear cell. The claims are also drawn to a method of determining the presence of a tumor cell in an individual by obtaining a sample from the individual and detecting the level of peripheral blood mononuclear expression of SEQ ID No 81. The claims are also drawn to a method of determining the presence of a tumor cell by obtaining a sample from an individual and detecting the level of peripheral blood mononuclear cell expression of SEQ ID No 81 and by providing a diagnostic kit, obtaining a sample, and quantifying an expression product of a marker gene.

Guidance in the Specification

The specification asserts a change in expression product of a marker gene is indicative for whether a treatment is effective or not by the level of expression, which can be enhanced or reduced. The specification asserts the expression product of the marker gene is preferably

quantified and the level of expression product of marker genes can vary from patient to patient (see paragraph 10, page 4). The specification further asserts that a very sensitive expression detection system will typically detect expression product where a less sensitive system detects no expression product and a person of skill in the art is well capable of designing the most appropriate expression detection system to practice this preferred embodiment (see paragraph 10, page 5), however the specification does not teach the most appropriate expression detection system to detect expression of a marker gene. The specification asserts that in a preferred embodiment the tumor comprises Kaposi's sarcoma. The specification asserts that Kaposi's sarcoma is a disease of proliferating blood vessels and is very much suited for identifying marker genes involved in angiogenesis (see paragraph 12, page 5). The specification asserts further that angiogenic mechanism causing the lesions of Kaposi's Sarcoma is an interplay of viral and cellular gene expression and is poorly understood in terms of which genes are involved and what controls their expression (see paragraph 13, page 6). Further, the angiogenic proliferation of Kaposi's sarcoma is likely to be universal in angiogenesis and marker genes for angiogenesis are very suitable for determination of whether a treatment of Kaposi's sarcoma is effective (see paragraph 13, page 6).

The specification asserts a method of determining gene expression patterns in Kaposi's Samoa by serial analysis of gene expression (see paragraph 18, page 6). The specification asserts that the use of a nucleic acid comprising a sequence of Seq ID No 81 can be used as a detection marker for the process of angiogenesis in the course of regenerative treatment and changes in expression level of the detection marker indicate active growth of blood vessels (see paragraph 23, page 9). However, the specification does not teach how much change in

expression level of the detection marker indicates active growth of blood vessels. The specification further asserts that it is possible to monitor a specific status of an individual, the presence of a disease, or developing the disease (see paragraph 26, page 10). However, the specification further states the absence of a marker gene in a sample can be indicative for the presence of a disease or for danger of developing the disease (see paragraph 26, page 10) and that a decreasing amount of expression product in samples in a specific time period can indicate – either beneficial or harmful – process. The specification does not give any guidance on how to determine if the absence of the marker gene is indicative of disease, developing disease, or not having the disease at all or how to determine if the expression amount is beneficial or harmful.

The specification states the invention provides a method for determining whether an individual comprises a non-hemopoietic cell from a patient comprising an altered amount of an expression product of a marker gene as compared with a reference value (see paragraph 30 , page 12). However the specification provides no guidance how to determine if the altered amount of expression is indicative of the presence of a non-hemopoietic cell.

Working Examples

The specification teaches obtaining SAGE libraries of two patients with Kaposi's Sarcoma that were not treated and obtaining SAGE libraries of one patient after 24 hours of chemotherapy treatments and after 48 hours of treatment and determining the expression profiles of the samples (see page 14-16, examples 1-3). The specification teaches determining markers in skin samples of 5 different samples with Kaposi Sarcoma and 2 control samples without Kaposi's Sarcoma (see example 10, page 33 and figure 19). The specification teaches determining gene expression levels of sequences in peripheral blood mononuclear cell sample by

taking blood samples of 4 different patients with Kaposi's Sarcoma and two different patients without Kaposi's Sarcoma and analyzing expression levels (see example 11, page 41 and figure 20). However, the specification provides no indication as to whether the results were statistically significant such that the skilled artisan would be able to predictably correlate the results with the presence of a tumor cell, diagnosis of disease, or efficacy of treatment of disease.

The following are unclear from the teachings in the specification. The specification envisions hypothetical situations where a gene marker expression could determine the presence of a target cell or efficacy of treatment of a target cell associated with any disease. The specification appears to be conceiving of possible scenarios where the expression level could be either enhanced or decreased and that these results would indicate the presence – or absence – of a target cell and specifically and tumor cell however, it is unclear how one of skill in the art would determine the level of expression necessary to determine the presence of the specific cell. Specifically, the specification does not teach how to determine how much of a change in expression in Seq ID No 81 would indicate the presence of a target cell of any disease. Further, it is unclear if a change in expression of Seq ID No 81 would even indicate the presence of a target cell or how this change would relate to the efficacy of treatment of the target cell. The specification does not teach how to detect a marker gene that is indicative of any disease, developing disease, or not having the disease at all nor does it teach how to determine if the expression amount of the marker gene is beneficial or harmful. Further, it is unclear how to determine if the altered amount of expression is indicative of the presence of a non-hemopoietic cell. The specification lacks guidance on how the specific marker genes found in the study on Kaposi's sarcoma are suitable for determining if any treatment is effective and further it is

unclear how the gene markers relate to any disease or angiogenesis. It is unclear how one of skill in the art would design the most appropriate expression detection system to practice this preferred embodiment and assess the efficacy of the results of the embodiments.

The unpredictability of the art and the state of the prior art

There is a large body of knowledge in the prior art related to angiogenesis in general, and their association with tumor identification, as well as drug or therapeutic response. However, the art is highly unpredictable with regard to the angiogenic status of an individual or the routine assessment of the effect of a given treatment on tumor angiogenesis. Post filing art, Ruegg et al. teaches that to date there is no validated laboratory test to determine the angiogenic status of an individual patient and to routinely assess the effect of a given treatment on tumor angiogenesis (Current Molecular Medicine 2003, 3, pp. 673-691, see specifically page 685, 2nd column, 1st paragraph). It is unpredictable whether any such marker would be associated with angiogenesis and accurately determine a disease state, a physiological state, or drug metabolism or response. For example, Ruegg et al. teaches that developing a test is an enormous challenge with far reaching clinical implications and many reputable academic and pharmaceutical research laboratories are currently engaged in such effort. Ruegg et al. teach that developing a marker specific to a tumor vasculature would require identification of a new marker, from four different samples: the angiogenic endothelial cell, the plasma from same patient, endothelial cells from corresponding healthy tissues from same patients and/or healthy donors, and plasma from healthy individuals (see page 685, 2nd column, 2nd paragraph and figure 4). Even in a case where an association between a particular transcription profiles and an angiogenic disorder, Kaposi's Sarcoma (KS), was found to exist, such as with the applicant's own work (van der

Kuyl et al., BMC Cancer 2002 2(1):21) of comparing a patient with AIDS-KS and the effectiveness of treatment by determining a mRNA profile after 24 and 48 hours after therapy to two untreated patients, van der Kuyl et al. found that based on genetic expression profiles the libraries of the treated patient after 48 hours were more closely related to patients untreated than the treated patient after 24 hours (see page 7, 2nd column 1st paragraph), suggesting that the association between transcription profiles, angiogenic disorder, and treatment prognosis is unpredictable. Further, applicant's own post filing art (Cornelissen et al, BMC Cancer 2003 3:7), teaches a study of semi-quantative PCR analysis of six genes profiles that were found to have increased expression in KS tissue samples and found only one of the six gene expressions had a $P<0.05$ compared to normal skin tissue (see page 9, 1st column, 1st full paragraph and figure 3). Further, figure 3 shows that the other five gene expression profiles of the KS tissue samples are within error of the normal skin tissue samples (see Figure 3, page 12). Cornelissen et al. specifically teaches that it is unpredictable to determine based on gene expression of KS samples an association between angiogenic disorder, diagnosis, and treatment efficacy since Cornelissen et al. shows that normal tissue samples are within error of KS tissue samples. Additionally, van der Kuyl et al. shows a difference in gene expression profiles after 24 and 48 hours after treatment of the same patient, which indicates the unpredictability of determining if a treatment will be effective based on gene expression.

In the instant case, the specification appears to envision scenarios where the marker genes expression level could be used to indicate the presence – or absence – of a tumor cell however, it is unclear how one of skill in the art would determine the level of expression necessary to determine the presence of the tumor cell or efficacy of treatment considering the unpredictably of

the art. The prior art, along with applicant's own post filing art, supports the unpredictability of this area of technology.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Quantity of Experimentation

Given the lack of guidance in the specification with regard to the determining the amount of change in expression of gene markers to determine the presence of a tumor cell and a non-hemopoeitic cell, efficacy of treatment, and relation of the marker genes to angiogenesis in any individual and along with the evidence in the art with regard to the variance of determining treatment efficacy by gene expression specifically for angiogenesis, the quantity of experimentation in this area is extremely large. The skilled artisan would have to perform an extremely large study in different populations to determine if in fact there was either an association between the expressed gene in individuals with Kaposi's Sarcoma or any other angiogenic disease relative to individuals without any angiogenic disease. The results of such a study are completely unpredictable as evidence by the evidence presented in applicant's own post filing date art (which reflects the current state of the art) with regard to the gene expression profile of a Kaposi's Sarcoma patient to comparison of normal gene expression profile without the disorder and the variance in expression levels after treatment. Further, post filing art Ruegg et al. teach developing a test to determine the angiogenic status of an individual is an enormous challenge (see Figure 4). The claims are broadly drawn to method of determining efficacy of treatment in a target cell, determining whether an individual possesses a non-hemopoetic tumor cell and/or site of angiogenesis and determining the presence of a tumor cell. To practice the

invention as broadly as it is claimed, the skilled artisan would have to determine a marker gene that would be specific for the tumor cell and determine how much expression would be associated with the tumor cell to determine if the individual would posses the tumor cell. Further, the skilled artisan would have to determine the change in expression values to assess the efficacy of treatment on the tumor cell. Such experiments are unpredictable, as evidence by the post filing date art and require extensive experimentation and a large research study with a large sample size. The skilled artisan would have to screen each gene profile expression to determine those that possess a tumor cell in all populations. The skilled artisan would have to perform an extremely large amount of trial and error analysis in a large study to determine if such expression profiles would predictably determine a susceptibility or diagnosis to a tumor cell. Given the lack of guidance in the specification and the conflicting evidence in the art, such analysis is replete with unpredictable experimentation and is considered undue.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-3, 9-10, 19, and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Sager et al. (US Patent 5688641 Nov 1997).

With regard to claim 1-3, and 19 Sager et al. teach a method of determining the presence of cancerous cells in a tissue by obtaining from a patient a tissue sample comprising cancerous

cells and contacting the nucleic acid probe under high-stringency hybridizing conditions with RNA (see column 4, lines 10-15 and lines 22-30). Sager et al. also teach a method of treating cells with a variety of drugs to determine which drugs increase the level of expression of the candidate tumor suppressor gene product within these cells (see column 15, lines 65-67 and column 16, lines 1-5)

With regard to claims 9-10, Sager et al. teach a method of using a nucleic acid probe to determine the presence of a cancerous cell by obtaining a tissue sample potentially comprising cancerous cells, providing a second tissue sample containing cells substantially non-cancerous (reference value) and hybridizing the samples with a nucleic acid probe (see column 4, lines 22-30). Sager et al. teach that comparing the amount of hybridization of the first sample with the amount of hybridization of the second tissue sample (see column 4, lines 30-34).

With regard to claim 29, Sager et al. teach a diagnostic assay of determining the presence of cancerous cells by the level of candidate tumor suppressor gene product in a biological fluid (blood or urine) (see column 5, lines 21-25).

10. Claims 1-3, 9-11, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Miles et al. (US Patent 5470824 Nov 1995).

With regard to claims 1-3, 9, and 11, Miles et al. teach a method of obtaining cell lines from Kaposi's Sarcoma lesions of patients with AIDS and determining the presence of IL-6 and IL-6 receptor RNA in the cells by slot-blot hybridization analysis (see column 2, lines 33-42). Miles et al. teach any candidate as an agent for intervention in the progress of Kaposi's Sarcoma can be evaluated and identified as a successful active agent by examining the effect of the

candidate anti-Kaposi's sarcoma agent on the level or function of IL-6 is suitable cells (see column 4, lines 28-32).

With regard to claim 10, Miles et al. teach a method of assessing effectiveness of a candidate agent by administering the candidate only to select lesion and to inject the alternate lesions with control (see column 6, lines 38-40).

With regard to claim 19, Miles et al. teach a method of determining the presence of IL-6 in cells by slot-blot hybridization (see column 2, lines 33-42).

11. Claims 1-3, 6, 9-11, 19, and 21-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Brown et al. (Am. J. of Pathology vol. 156, no 6, June 2000).

With regard to claims 1-3, 9-10, 11 Brown et al. teach a method of obtaining biopsies from Kaposi's sarcoma (KS) (instant claim 11) lesions and normal skin (control, reference value, instant claim 10) and hybridize RNA probes of five different proteins to the isolated tissue samples and quantified mRNA expression in KS (instant claim 9) (see In Situ Hybridization, page 2180, 1st column and Table 1).

With regard to claim 6, Brown et al. teach RNA probes hybridized to proteins Tie-1 and Tie-2 (see table 1) and Tie-1 and Tie-2 are reported to play important roles in embryonic blood vessel development (see column 1, 1st full paragraph, page 2182).

With regard to claim 19, 21-22, Brown et al. teach obtaining biopsies from two patients and a control biopsies of normal skin and teach a strong expression of aniogpoietin-2, Tie1 and Tie2 in Kaposi's sarcoma and angiosarcoma (see 2nd column, 1st paragraph, page 2181).

12. Claims 1-3, 6, 9-11, 19, 21-22, 24, 29-30 rejected under 35 U.S.C. 102(b) as being anticipated by Sirianni et al. (Blood volt 91, No 3, Feb. 1 1998, pp 968-976).

With regard to claims 1-3, 11, 19, 21, and 29-30, Sirannin et al. teach isolation of PBMC from patients affected with Kaposi's sarcoma (see page 969, 1st column, last two paragraphs). Sirannin et al. teach analysis of gene expression by antibody staining, measurement of cytokine, and detection of HHV-8 nucleic acid sequence by hybridization (see page 969, 2nd column, last two paragraphs and page 970, 1st column, 1st paragraph).

With regard to claim 9, Sirannin et al. teach quantification of gene expression by immunophenotyping of TIL (see table 2, page 970).

With regard to claim 10, Sirannin et al. teach a group of 20 normal volunteers studied as a control for immunologic phenotyping and a group of 34 patients with skin disorders other than KS, studied as a control for cytokine production (reference value) (see page 969, 1st column, 5th paragraph).

With regard to claim 22, Sirannin et al. teach a method of determining the presence of gene expression of TIL by immunophenotyping of KS lesions (see table 2). KS is an angioproliferative disease (gene involved in angiogenesis) (see 1st sent. page 968)

With regard to claim 24, Sirannin et al. teach a method of determining the presence of HHV-8 hemopoeitic cells in PBMC cells (see column 2, 2nd full paragraph and table 4, page 973).

13. Claims 1, 4-5, 9-10, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by anticipated by Sonis et al. (Oral Oncology 36 (2000) 373-381).

With regard to claims 1, 9 and 19, Sonis et al. teach a method of treating hamsters with

ulcerative mucositis (target cell) with rhIL-11 from day –1 to day 14 (see page 374, section 2.3). Sonis et al. teach quantification (instant claim 9) of cytokine expression levels and immunohistochemical evaluation of IL-1β and keratin (see page 375, page 2.6.4 and 2.6.5).

With regard to claims 4-5, Sonis et al. teach the effect of rhIL-11 on inflammatory gene expression after 0 and 5 days (see figure 7, page 379). Sonis et al. teach the effect of rhIL-11 on epithelial cell differentiation by measuring keratin expression after 1 (within two days, instant claim 4) and 5 days (within one week, instant claim 5) (see figure 10, page 380).

With regard to claim 10, Sonis et al. teach a method of administering autologous hamster serum to a control group of hamsters (reference value) (see section 2.3, page 374).

Double Patenting

14. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

15. Claims 1-6, 9-10, 19, 21-22, 24, 29-30 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-6, 9-10, 19, 21-22, 24, 30 of copending Application No. 10/310677. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

For example, claim 1 is identical in scope compared to claim 1 of Application No.

10/310677. Although the terminology of instant claim 1 is not identical to claim 1 of application 10-310677, the terminology of "individual" in instant claim 1 has equivalent meaning to the term "subject" of claim 1 in application 10/310677. This is a double patenting rejection.

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 8, 11-12, 14-18, 20, 23, 31-33 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7-8, 11-12, 14-17, 20, 23, and 31-33 of copending Application No. 10/310677. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 7-8, 11-12, 14-17, 20, 23, and 31-33 of application 10/310677 is generic and coextensive in scope to all that is recited in instant claims 8, 11-12, 14-18, 20, 23, 31-33 of the pending application. That is claim 7-8 of Application No. 10/310677 falls entirely in the scope of instant claim 8, claim 11-12 and 14-17 of Application No. 10/310677 falls entirely in the scope of instant claim 11-12, 14-18, claim 20 and 23 of Application No. 10/310677 falls entirely in the scope of instant claim 20 and 23, and claim 31-33 of Application No. 10/310677 falls entirely in the scope of instant claim 31-33.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571) 272-2912. The examiner can normally be reached on M-F 10am-7pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is (573) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Jehanne Sitton
JEHANNE SITTON
PRIMARY EXAMINER
2/7/05

Sarae Bausch, PhD.
Examiner
Art Unit 1634